of lead on putative OA biomarkers. We examined whole blood Pb levels and OA biomarkers in African American and white women.
Methods: A total of 339 women in the Johnston County OA Project Metals Exposure Sub-study (mean age 62.5 (9.4) years, 35% African American) had available whole blood, serum, or urine samples for whole blood lead and biomarkers assessments. Whole blood lead was measured by inductively coupled plasma mass spectrometry at the Inorganic Toxicology laboratory, Division of Laboratory Sciences, National Center for Environmental Health, CDC, Atlanta, Georgia. Urine C-telopeptide fragments of type II collagen (CTX-II), cross linked N telopeptide of type I collagen (NTX-I), serum hyaluronic acid (HA) and cartilage oligometric matrix protein (COMP) were measured by commercially available kits. Radiographic knee OA (rKOA) was defined by Kellgren-Lawrence grades (2-4) with fixed-flexion posterior-anterior knee films. Pearson correlation coefficients were calculated between Log Pb and log of each biomarker. Analysis of covariance models were used to examine associations between blood lead levels and the 4 chosen biomarkers with log transformed biomarkers as outcomes, adjusted for age, race, BMI, and rKOA variables. Effect modification between log Pb and race were examined, with significance defined by p-values < 0.1 for interaction terms.
Results: Median Pb levels were 1.9 ug/dL (0.5-25.4) and were higher in African American women than white women ($p < 0.001$). In bivariate associations, log Pb was correlated with log CTX-II (r=0.14, p=0.009) and log NTX-I (r=0.22, $p<0.0001$), but not with log COMP or log HA (r= 0.07 and 0.06, respectively, $p>0.20$). In adjusted models, log Pb was associated with mean log CTX-II ($p = 0.007$), NTX-I ($p <0.001$), and COMP ($p = 0.036$), but not with mean log HA ($p = 0.9$). There were no notable race and log Pb interactions.
Conclusions: Mean blood Pb levels are associated with urine CTX-II, urine NTX-I, and serum COMP, but not serum HA in both African American and white women. These data suggest that Pb has an effect not only on bone collagen, but also on type II collagen and non-collagenous matrix proteins. Potential effects of Pb in the pathogenesis of OA, then, are likely to be related to alterations in these factors, but not to effects on synovial inflammation. We are planning further studies to delineate how Pb may affect joint structures and how other factors such as menopause, hormone replacement therapy, and bone density, might influence these associations.

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EFFECT OF OVER-THE-COUNTER DOSES OF NAPROXEN SODIUM ON INHIBITION OF PLATELET CYCLOOXYGENASE-1 IN HEALTHY VOLUNTEERS

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Purpose: Data from a meta-analysis of randomized controlled trials suggest that 1 g of naproxen is not associated with deleterious cardiovascular outcomes, perhaps due to its antiplatelet effects. The effect of over-the-counter (OTC) doses of naproxen on platelets is unknown. We compared the antiplatelet effects of OTC doses of naproxen sodium (NAPSO) with a prescription (Rx) dose of NAPSO and low-dose enteric-coated aspirin (EC-ASA).
Methods: Single-center, randomized, open-label, placebo-controlled, 2-period crossover trial in healthy male and female subjects. Subjects were administered 1 of 3 regimens of NAPSO (NAPSO 220 mg twice daily (bid), NAPSO 220 mg 3 times daily (tid), or NAPSO 550 mg bid) or placebo for 7 days. After a washout period of at least 6 days, subjects were crossed over to receive EC-ASA 81 mg once daily for 7 days. The primary endpoint was inhibition of serum thromboxane B2 (TXB2), measured at trough (12 hours after the final dose of NAPSO) and 24 hours after final dose of EC-ASA. Inhibition of serum TXB2 was measured by a commercially available enzyme immunoassay.
Results: A total of 48 subjects were randomized [the intent-to-treat (ITT) population], and 41 (11 NAPSO 220 mg bid, 9 NAPSO 220 mg tid, 11 NAPSO 550 mg bid, 10 placebo) met the criteria for the evaluable population. Baseline characteristics were comparable among the 4 groups. NAPSO demonstrated an aspirin-like effect on platelet aggregation, as measured by inhibition of serum TXB2. The mean ($\pm$SD) degree of serum TXB2 inhibition was 97.9% ($\pm$ 3.20%) for NAPSO 220 mg bid and 99.4% ($\pm$ 0.77%) for NAPSO 220 mg tid. The inhibitory effects of these OTC doses of NAPSO were similar to the Rx dose of NAPSO 550 mg bid [99.6% ($\pm$ 0.69%)]. The lower limit of a one-sided 95% CI test for non-inferiority (NAPSO or placebo versus ASA) for each treatment was -1.7% for NAPSO 220 mg bid, -0.2% for NAPSO 220 mg tid, -0.6% for NAPSO 550 mg bid, and -75.8% for placebo (Table 1). All doses of NAPSO were not inferior to EC-ASA 81 mg. Results were confirmed in an analysis of the ITT population.
Conclusions: Over-the-counter doses of NAPSO produced an antiplatelet effect similar to low dose EC-ASA and Rx dose NAPSO, as measured by inhibition of serum TXB2.

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HYALURONAN-LINKED INTER-α-TRYPSIN INHIBITOR HEAVY CHAIN (SHAP), INTERLEUKIN 8, MMP-3 AND HYALURONAN IN HUMAN SYNOVIAL FLUID AND SERUM IN OSTEOARTHRITIS, JOINT INJURY AND INFLAMMATION

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Purpose: Inter-α-trypsin Inhibitor (IαI) occurs in plasma and has protease inhibitory activity. Heavy chains of IαI can bind covalently to hyaluronan (HA) to form a serum derived hyaluronan associated protein, SHAP, releasing bikunin. The transfer of IαI heavy chain to HA is catalyzed by enzyme factors such as TNFα-stimulated gene 6 protein (TSG-6). SHAP potentiates CD44-mediated leukocyte adhesion to hyaluronan substratum, and has putative roles in HA cross-linking and inflammation.

P96 – Table 1. Percent Inhibition of Serum Thromboxane (TXB2) trough/steady state*

	Period 1 Mean (SD)	Period 2 (EC-ASA 81mg) Mean (SD)	Period 1 - Period 2 Mean Difference(SD)	Lower Limit Non-inferiority (5%) One-sided 95% CI
NAPSO 220 mg bid (440 mg) (n=11)	97.9 (3.20)	98.4 (2.54)	-0.5 (2.20)	-1.7
NAPSO220 mg tid (660 mg) (n=9)	99.4 (0.77)	98.0 (2.57)	1.3 (2.46)	-0.2
NAPSO550 mg bid (1100 mg) (n=11)	99.6 (0.69)	97.2 (5.65)	2.3 (5.46)	-0.6
Placebo (n=10)	47.3 (41.03)	99.2 (1.01)	-51.9 (41.18)	-75.8

*Blood drawn 24 hrs after last ASA dose and 12 hrs after last NAPSO dose at steady state